NEPHROLOGY

When to suspect Renal disorders?

1. Uremic features : (Loss of excretory function)
   - Encephalopathy/Convulsions/Dementia
   - Pericarditis/Shock (Direct suppression of Myocardium)
   - Gastritis/Anorexia
   - Myopathy/Neuropathy
   - Loss of Libido/Infertility
   - Coagulopathy (Platelet aggregation defect → Deranged BT)

Neuropathy is present in 90% CKD patients. It is the reason to poor response to dialysis.

2. Water and Acid Base Balance defect : (Homeostatic function loss)
   - Oliguria (U.O < 400ml/day)
   - Anuria (U.O < 100ml/day)
   - Polyuria (U.O. >3L/day)

   Metabolic Acidosis : NAGMA In Early CKD and RTA &
   HAGMA in Late CKD (GFR < 25ml/min)

3. Anaemia/Metabolic bone disease: (Hormonal function loss)

Osteitis Cystica Fibrosa (MC) : Due to secondary hyperparathyroidism
Adynamic Bone Disease : Due to remodelling bone defect
Osteomalacia: Due to Active Vitamin D deficiency)

Anemia is Normocytic type and happens on kidney disease of >6 months duration.

A.K.I	Parameters	C.K.D
PRESERVED	Cortico-Medullary Differentiation on USG*	LOST
Normal / Enlarged	SIZE-USG	Normal / SHRUNKEN
Fluctuates depends on cause	Compare Uosm & Posm	Isothenuria (Same as Posm)
Hyaline	CASTS	Broad/Waxy
Uncommon	ANAEMIA	Common
Absent	CKD-MBD	Maybe PRESENT

Diagnosis:

AKI: Using KDIGO GUIDELINES*

- Urine output <=0.5ml/kg/hour >= 6 consecutive hours
- Rise in Creatinine >= 0.3mg/dl from baseline <= 48hours
- Rise in Creatinine >= 1.5*Baseline <= 7 days

CKD

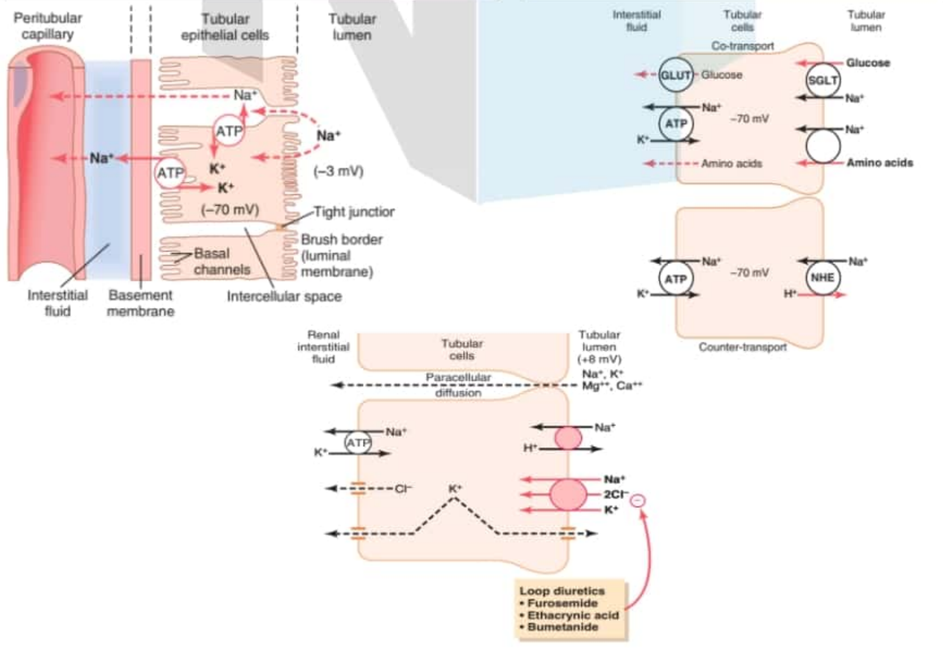
- Presence of kidney damage or decreased kidney function for > 3 months.
- The persistence of the damage or decreased function for atleast 3 months is necessary to differentiate from AKI

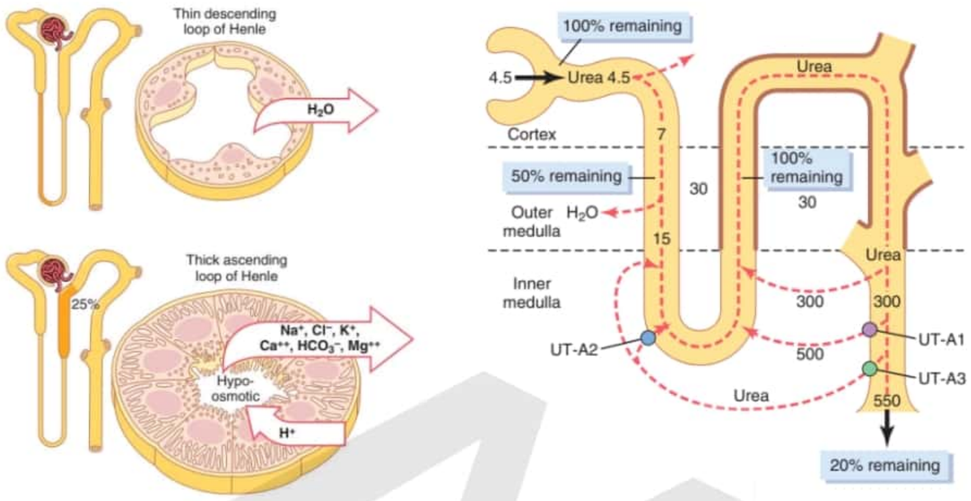
TABLE 37–4 Factors affecting the glomerular filtration rate.

Changes in renal blood flow
Changes in glomerular capillary hydrostatic pressure
Changes in systemic blood pressure
Afferent or efferent arteriolar constriction
Changes in hydrostatic pressure in Bowman capsule
Ureteral obstruction
Edema of kidney inside tight renal capsule
Changes in concentration of plasma proteins: dehydration, hypoproteinemia, etc (minor factors)
Changes in K_f
Changes in glomerular capillary permeability
Changes in effective filtration surface area

TABLE 37–5 Transport proteins involved in the movement of Na^+ and Cl^- across the apical membranes of renal tubular cells.*

Site	Apical Transporter	Function
Proximal tubule	Na/glucose CT	Na^+ uptake, glucose uptake
	Na^+/P_i CT	Na^+ uptake, P_i uptake
	Na^+ amino acid CT	Na^+ uptake, amino acid uptake
	Na/lactate CT	Na^+ uptake, lactate uptake
	Na/H exchanger	Na^+ uptake, H^+ extrusion
	Cl/base exchanger	Cl^- uptake
Thick ascending limb	Na–K–2Cl CT	Na^+ uptake, Cl^- uptake, K^+ uptake
	Na/H exchanger	Na^+ uptake, H^+ extrusion
	K^+ channels	K^+ extrusion (recycling)
Distal convoluted tubule	NaCl CT	Na^+ uptake, Cl^- uptake
Collecting duct	Na^+ channel (ENaC)	Na^+ uptake





Hypervolemia in AKI

- Diuretics may be used to relive hypervolemia among patients with AKI who are not anuric.
- Loop diuretics (Na-K-2Cl inhibitor) are the preferred agents as they provide a greater natriuretic effect than thiazide diuretics.
- Dosing of loop diuretics varies inversely with GFR.
- Diuretics are generally given intravenously rather than orally since the oral absorption is impaired d/t decreased intestinal perfusion and motility and mucosal edema.
- Furosemide is the preferred agent and starting dose is 80 mg IV
- If there is no increase in urine output, dose can be increased up to 200 mg or a thiazide diuretic can be added.
- Lack of response to a 200 mg dose of IV furosemide or equivalent with or without a thiazide diuretic, may suggest the need for extracorporeal removal of excess volume.

Hypervolemia in CKD

- Patients with CKD and volume overload respond to the combination of dietary sodium restriction and diuretic therapy, usually with a loop diuretic given daily.
- Sodium intake should be restricted to < 2g/day unless contraindicated.
- Water restriction is indicated only if there is a problem with hyponatremia.
- In cases if refractory edema, thiazides like metolazone can be added.
- Patients of CKD with reduced GFR require higher loop diuretic doses to achieve the maximum effect.
- In CKD, the upward dose adjustment varies inversely with the estimated GFR
- Dosing should not exceed the maximal recommended daily dose because of increased risk for toxicity(particularly ototoxicity, which may be irreversible).

- Ototoxicity primary occurs with high dose IV therapy or at low doses in patients with kidney function impairment or concurrent use of other ototoxins such as aminoglycosides.
- The risk of ototoxicity may be lower with continuous IV infusion rather than bolus therapy.
- Other Side effects are:
  - Hypokalemia
  - Metabolic alkalosis
  - Hypovolemia, hypotension
  - Hyperuricemia
  - Hyponatremia

Hyperkalemia in CKD

- Dietary restriction of potassium.
- The use of kaliuretic diuretics e.g. loop diuretics, thiazides.
- Dose reduction or avoidance of potassium retaining medications like ACEI or ARBs
- Potassium binding raisins such as sodium polystyrene or patiromer can promote potassium loss through the GI tract.
- Intractable hyperkalemia is an indication (although uncommon) to consider institution of dialysis in CKD patient.
- Loop and thiazide diuretics increase potassium loss in the urine of patients with normal or mild to moderately impaired renal function, particularly when combined with saline hydration to maintain distal sodium delivery and flow.
- Patients with persistent hyperkalemia typically have impaired renal potassium secretion, and not kaliuretic response to diuretic therapy Is not useful.

Loop diuretics in Nephrotic syndrome

- Most patients respond well to loop diuretics but drug effect reduces in usual dose.
- The degree of protein-binding is reduced with hypoalbuminemia, resulting in a larger extravascular space of distribution and a slower rate of delivery to the kidney
- Higher doses are required in patients with nephrotic syndrome as compared to other edematous disorders

Anemia In CKD

- Anemia is common among chronic kidney disease (CKD) patients
- For most CKD patients, initiate treatment with erythropoiesis-stimulating agents ESAs when the hemoglobin (Hb) level is <10 g/dL, providing the transferrin saturation (TSAT) is >25 percent and ferritin >500 ng/mL

Anemia In CKD

- To patients with TSAT ≤25 percent and ferritin ≤500 ng/mL, administer iron before giving an ESA since they may respond to iron with an increase in Hb.
- Exceptions of ESA therapy are patients with malignancy, or who have had a stroke since such patients may be at higher risk for adverse effects from ESAs

Anemia In CKD

- ESA treatment is preferably given subcutaneous rather than intravenous route.
- Epoetin and darbopoetin are commonly used agents.
- Current practice is to target a hemoglobin concentration of 10.0–11.5 g/L

Case 1: 10 yr-old boy presents to the OPD with Short stature and Rickets. He gives history of recurrent episodes of loin pain with hematuria. Urine shows Eumorphic RBC on microscopy. USG revealed Nephrocalcinosis. ABG revealed Metabolic Acidosis with Normal Plasma AG and High Urinary AG. His potassium levels were low. What is the diagnosis?

Dx: Distal/Type 1 RTA

Approach to Hematuria

Step 1: Confirm "Significant Hematuria"

- Gross hematuria
- > 100 RBC/hpf on single occasion
- >3 - <100 RBC/hpf on >= 3 occasions

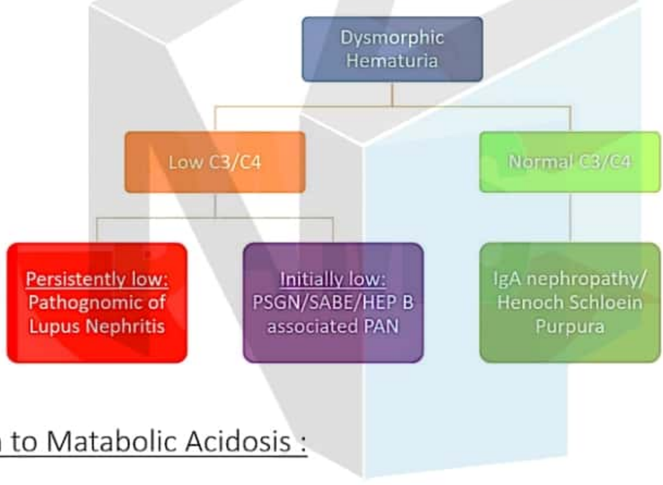
In significant Hematuria : RBC Morphology

EUMORPHIC (MC)
(S/o Collecting system defect)

Causes:
- Urinary infection/Cystitis (MC)
- Calculi
- Coagulopathy
- Carcinoma Bladder

DYSMORPHIC (RARE)
(S/o of Glomerulonephritis

Causes further classified based on C3/C4 levels

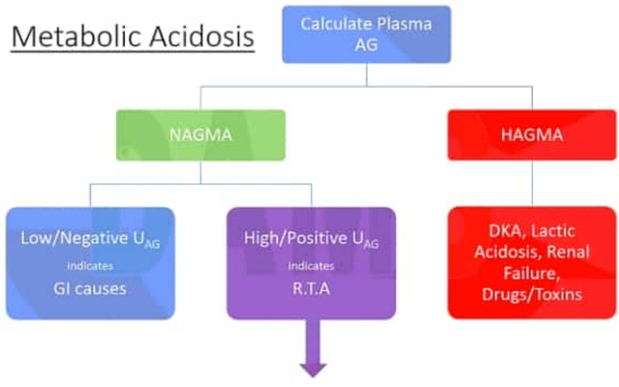


Approach to Matabolic Acidosis :

Plasma Anion Gap = (Na+) – (Cl- + HCO3--)

Normal Anion gap is 12 meQ

Urinary Anion Gap = $(U_{Na+} + U_{K+}) - (U_{Cl-})$



R.T.A

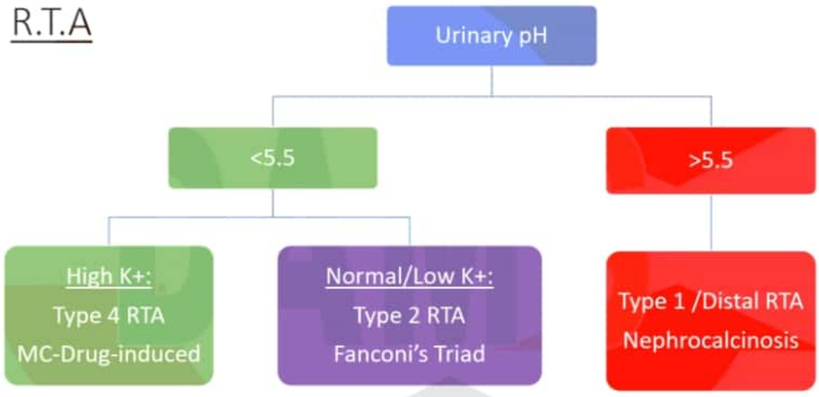


TABLE 39–1 H^+ concentration and pH of body fluids.

		H^+ Concentration		
		mEq/L	mol/L	pH
Gastric HCl		150	0.15	0.8
Maximal urine acidity		0.03	3×10^{-5}	4.5
Plasma	Extreme acidosis	0.0001	1×10^{-7}	7.0
	Normal	0.00004	4×10^{-8}	7.4
	Extreme alkalosis	0.00002	2×10^{-8}	7.7
Pancreatic juice		0.00001	1×10^{-8}	8.0

Henderson – Hasselbalch equation

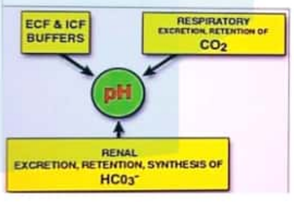
- $pH = -\log_{10}[H^+]$ (pH units)
- $pK = -\log_{10} K$ (pH units). This is equilibrium constant
- $[A^-]$ = Concentration of base form of buffer (mEq/L)
- [HA] = Concentration of acid form of buffer (mEq/L)

$$pH = pK + \log \frac{[A^-]}{[HA]}$$

Acid production in the body

1. Volatile acid = CO_2 itself is not an acid but it reacts with water to form carbonic acid
2. Fixed acid or non volatile acid = acids produced as a result of protein catabolism e.g. sulfuric acid, phosphoric acid, ketoacids, lactic acid, salicylic acids

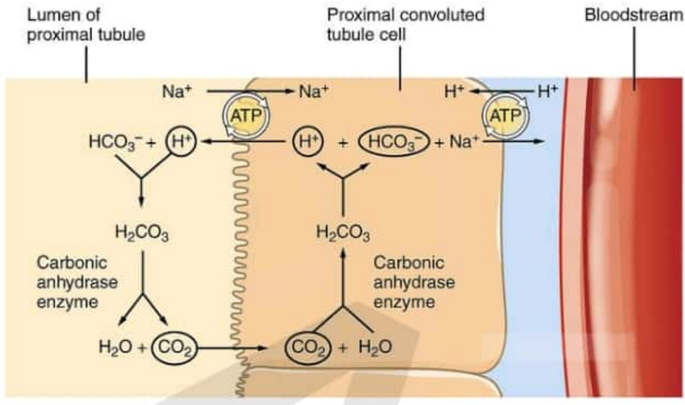
Three systems which maintain normal serum pH



Buffers in body fluids

- The buffers in the body fluid are both in ICF and ECF
- In ICF, are organic phosphates, Hb (Oxy Hb) and proteins.
- Lungs' role in acid-base regulation
  - Fast to respond
  - Respond to changes in CO2 levels
  - Rise in serum CO2 level causes a decreased pH
  - Fall in serum CO2 level causes an increased pH
- Kidney's role in acid base regulation
  - Slow to respond
  - Reabsorption and regeneration of HCO3

- Excretion of H+ that is produced as a result of protein and phospholipid metabolism



Renal excretion of H+

- The predominant buffers in the late DCT and CD are
1. Phosphate (PO_4^{3-})
2. Ammonia (NH_3)
- In late DCT and CD, H^+ is excreted either with phosphate or ammonia

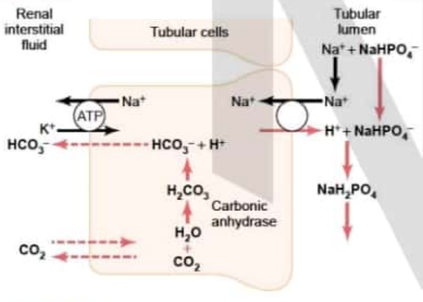
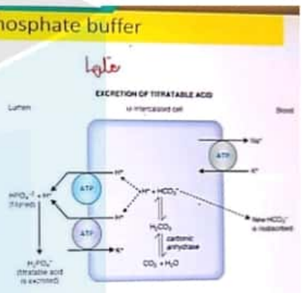


Figure 30–7

Buffering of secreted hydrogen ions by filtered phosphate ($NaHPO_4^-$). Note that a new bicarbonate ion is returned to the blood for each $NaHPO_4^-$ that reacts with a secreted hydrogen ion.

Phosphate buffer

- Phosphate is freely filtered by the glomerulus
- H^+ is excreted in the form of titratable acid $H_2PO_4^-$
- Mainly in the I cells of late DCT and CD
- The amount excreted depends on the urinary buffer (PO_4^{3-})



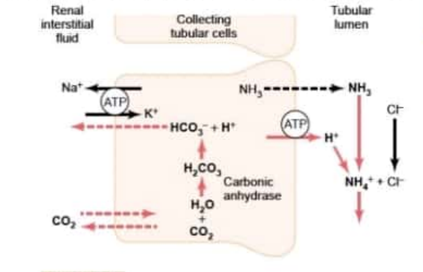


Figure 30–9

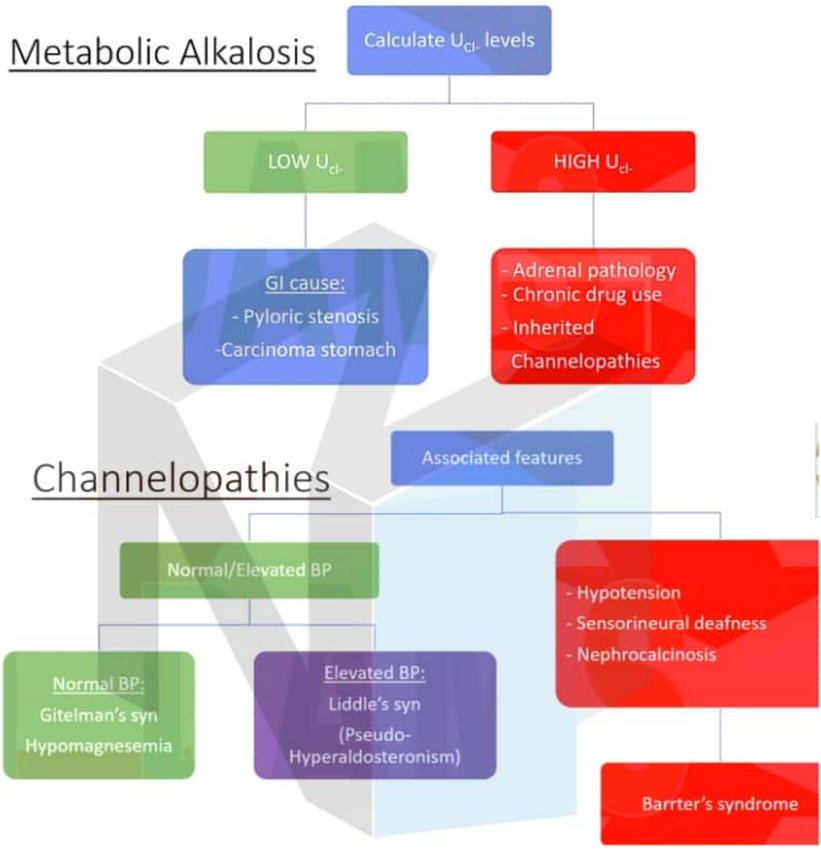
Buffering of hydrogen ion secretion by ammonia (NH_3) in the collecting tubules. Ammonia diffuses into the tubular lumen, where it reacts with secreted hydrogen ions to form NH_4^+, which is then excreted. For each NH_4^+ excreted, a new HCO_3^- is formed in the tubular cells and returned to the blood.

Ammonia buffer

- Ammonia is produced in renal tubular cells by the action of the enzyme glutaminase on the amino acid glutamine
- The ammonia combines with H+ to form ammonium which being ionized and is not lipid soluble does not pass back into the tubular cell
- The ammonium ion is lost in the urine, along with the hydrogen ion it contains

Case 2: 10 yr-old boy presents to the OPD with history of recurrent episodes of loin pain with hematuria. Urine shows Eumorphic RBC on microscopy. USG revealed Nephrocalcinosis. ABG revealed Metabolic Alkalosis with High UrinaryCl- levels Patient also suffers from deafness

Dx: Barrter's Syndrome



Case 3: 20 yr-old male presents to the OPD with history of hematuria. Urine shows Dysmorphic RBC. O/E: P-98/min, BP- 146/80mm of Hg Lab: Hb – 13.2gm/dl, Creatinine – 3.5mg/dl, USG – Normal size kidneys with Preserved CMD. Patient gives history of preceding sore throat.

Post-URTI GN: Nephritic syndrome

A. Focus on Latent period in such cases

- IgA nephropathy } – Within 1st week of URTI
- Post-Streptococcal GN(PSGN)

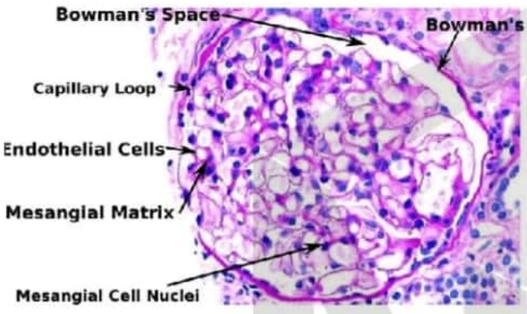
Post-URTI GN: Nephritic syndrome

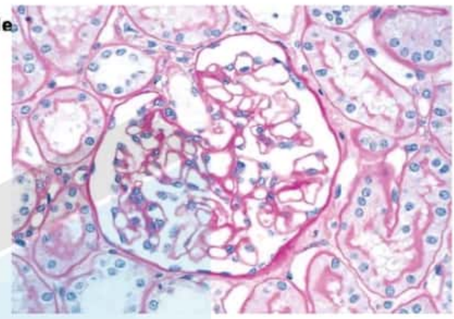
B. Focus on Serology/Antibody testing for Probable diagnosis:

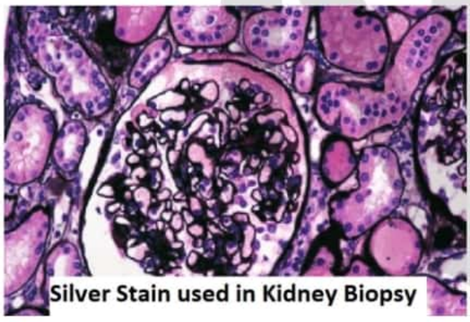
IgA Nephropathy
Elevated levels of IgA
Are pathognomic

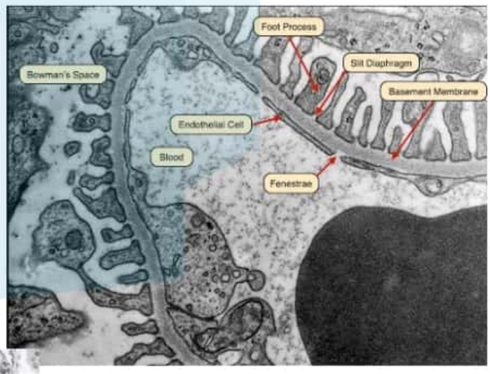
Post-Streptococcal GN(PSGN)
70%- Anti-DNAase Antibody
30-40% show ASO &
Anti-hyaluronidase antibody

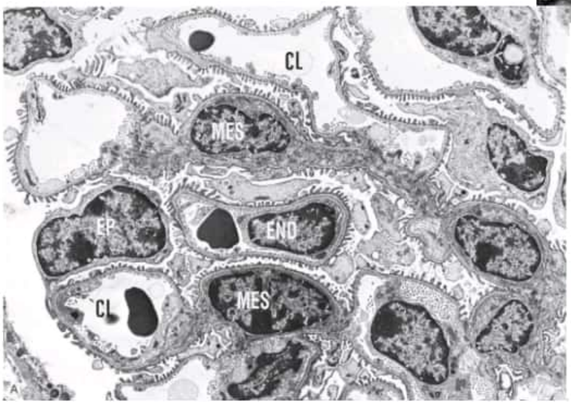
Histopathology of kidney











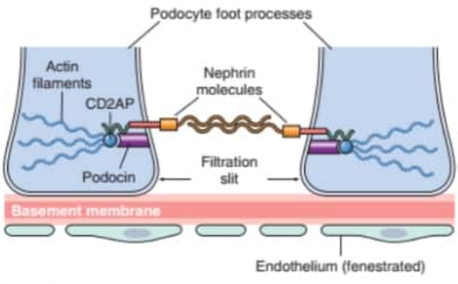
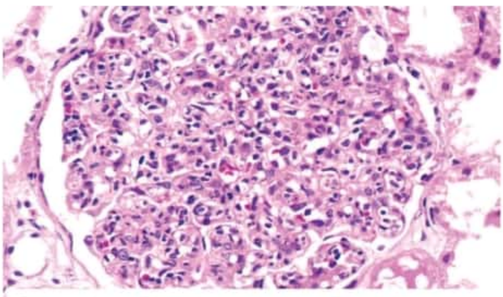


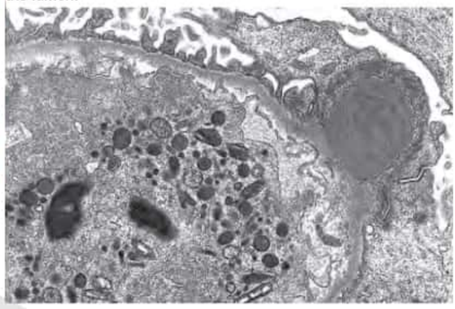
Figure 20-3 A simplified schematic diagram of some of the best-studied proteins of the glomerular slit diaphragm. CD2AP, CD2-associated protein.

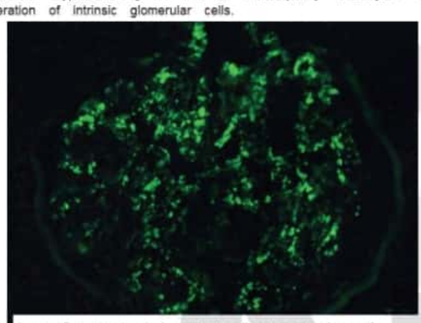
PSGN Findings



Glomerular hypercellularity is due to intracapillary leukocytes and proliferation of intrinsic glomerular cells.

Typical electron-dense subepithelial "hump" and a neutrophil in the lumen.





Immunofluorescent stain demonstrates discrete, coarsely granular deposits of complement protein C3 (stain for IgG was similar), corresponding to "humps"

IF pattern of coarse granules is also known as LUMPY BUMPY Pattern or STARRY SKY pattern.

ALL findings suggestestive of PSGN → Acute proliferative GN

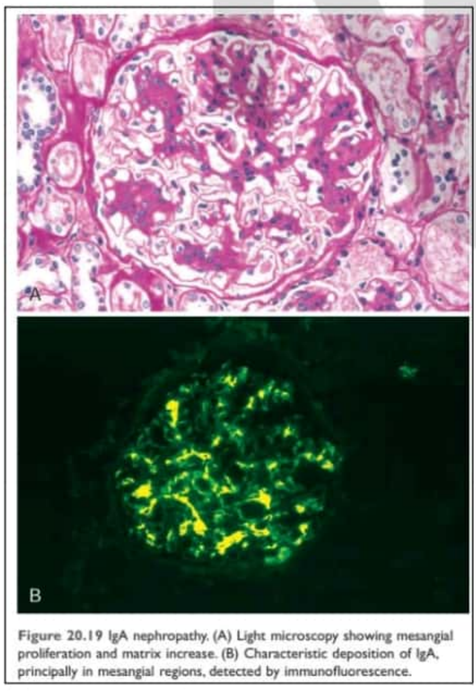


Figure 20.19 IgA nephropathy. (A) Light microscopy showing mesangial proliferation and matrix increase. (B) Characteristic deposition of IgA, principally in mesangial regions, detected by immunofluorescence.

Disease	Most Frequent Clinical Presentation	Pathogenesis	Glomerular Pathology		
			Light Microscopy	Fluorescence Microscopy	Electron Microscopy
Postinfectious glomerulonephritis	Nephritic syndrome	Immune complex mediated; circulating or planted antigen	Diffuse endocapillary proliferation; leukocytic infiltration	Granular IgG and C3 in GBM and mesangium; Granular IgA in some cases	Primarily subepithelial humps; subendothelial deposits in early disease stages
Crescentic (rapidly progressive) glomerulonephritis	Nephritic syndrome; rapid progression	Anti-GBM antibody mediated; immune complex mediated; ANCA mediated and unknown	Extracapillary proliferation with crescents; necrosis	Linear IgG and C3 in anti-GBM antibody mediated GN; granular IgG, other Igs, and/or complement in immune complex mediated GN; or no deposits in ANCA mediated GN	No deposits in anti-GBM and ANCA mediated GN; immune complexes at various locations in immune complex mediated GN
Membranous nephropathy	Nephrotic syndrome	In situ immune complex PLA_2R antigen in most cases of primary disease	Diffuse capillary wall thickening	Granular IgG and C3; diffuse	Subepithelial deposits
Minimal change disease	Nephrotic syndrome	Unknown; loss of glomerular polyanion; podocyte injury	Normal; lipid in tubules	Negative	Effacement of foot processes; no deposits
Focal segmental glomerulosclerosis	Nephrotic syndrome; non-nephrotic proteinuria	Unknown Ablation nephropathy Plasma factor (?); podocyte injury	Focal and segmental sclerosis and hyalinosis	Focal; IgM + C3 in many cases	Effacement of foot processes; epithelial denudation
Membranoproliferative glomerulonephritis (MPGN) type I	Nephritic/ nephrotic syndrome	Immune complex	Mesangial proliferative or membranoproliferative patterns of proliferation; GBM thickening; splitting	IgG ++ C3; C1q ++ C4	Subendothelial deposits
Dense-deposit disease (MPGN type II)	Hematuria Chronic renal failure	Acquired or genetic dysregulation of the alternative complement pathway	Mesangial proliferative or membranoproliferative patterns of proliferation; GBM thickening; splitting	C3; no C1q or C4	Dense deposits
IgA nephropathy	Recurrent hematuria or proteinuria	Unknown	Focal mesangial proliferative glomerulonephritis; mesangial widening	IgA ± IgG, IgM, and C3 in mesangium	Mesangial and paramesangial dense deposits

ANCA, Antineutrophil cytoplasmic antibodies; GBM, glomerular basement membrane.

Case 4: 20 yr-old male presents to the OPD with history of hematuria. Urine shows Dysmorphic RBC. O/E: P-98/min, BP- 146/80mm of Hg Lab: Hb – 13.2gm/dl, Creatinine – 3.5mg/dl, USG – Normal size kidneys with Preserved CMD Patient gives history of preceding sore throat. There is history of hemoptysis with increase in DLCO

Pulmonary Renal syndromes: Nephritic G

B. Focus on Serology/Organ involvement for Probable diagnosis:

Goodpasture's syndrome (GPS)	Vasculitis syndromes
70% have Anti-GBM antibodies (Antibody against the Alpha-3 Subunit of Type IV collagen.)	70% are ANCA positive (Mimics lung and kidney involvement of GPS)
Only 2 organs are affected.	BUT OTHER ORGANS involved

NEPHRITIC Syndrome

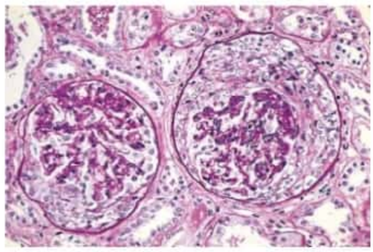


Figure 20-10 Crescentic glomerulonephritis (PAS stain). Note the collapsed glomerular tufts and the crescent-shaped mass of proliferating parietal epithelial cells and leukocytes internal to Bowman capsule. (Courtesy

PULMONARY RENAL SYN – D/D :

- Goodpasture's syndrome
- ANCA positive Vasculitis syndromes.
- Henoch Schloein Purpura

Nephritic syndromes are at higher risk of progressing to RPGN

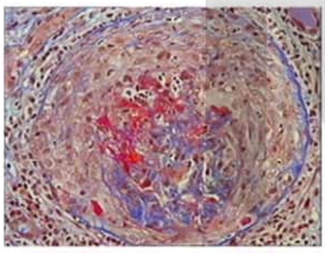
Type I (Anti-GBM Antibody)
Renal limited Goodpasture syndrome
Type II (Immune Complex)
Idiopathic Postinfectious glomerulonephritis Lupus nephritis Henoch-Schönlein purpura IgA nephropathy Others
Type III (Pauci-Immune)
ANCA-associated Idiopathic Granulomatosis with polyangiitis (formerly Wegener granulomatosis) Microscopic polyangiitis

Type 1 – IF: Linear Deposits

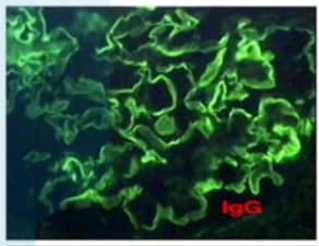
Type 2 – IF : Granular deposits

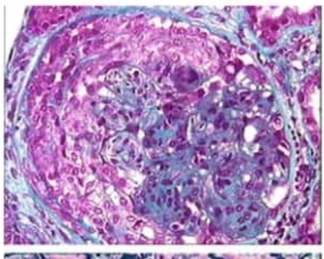
Type 3- IF: No deposits

 # Wire Loop lesions (subendothelial deposits) are seen in Class 4 Lupus Nephritis

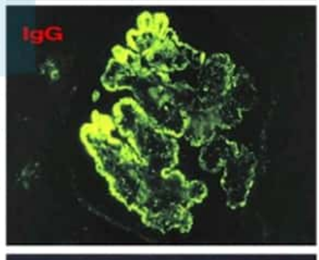


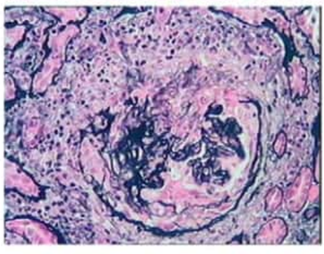
TYPE 1
Anti-GBM (linear IF)
- with alveolar haemorrhage (Goodpasture)
- without alveolar haemorrhage (anti-GBM GN)



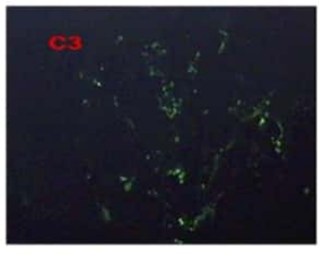


TYPE 2
Immune-complexes (granular IF)
- post-infective (post-streptococcal)
- secondary to SLE, HSP, Cryo
- complicating primary GN
- idiopathic



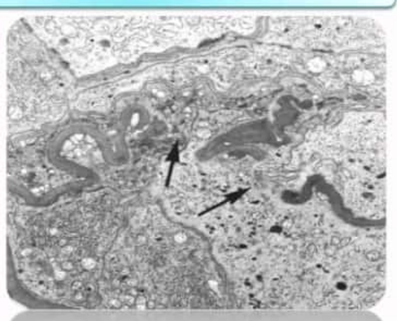


TYPE 3
ANCA (pauci-immune)
- Wegener's granulomatosis
- microscopic polyangiitis
- renal limited vasculitis
- Churg-Strauss syndrome



RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS

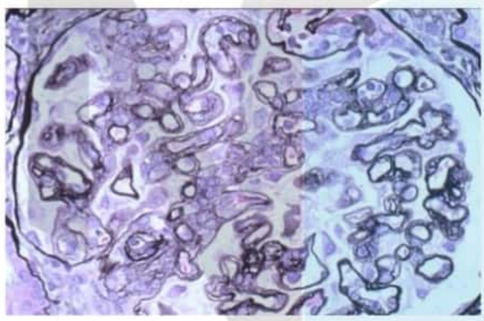
ELECTRON MICROSCOPY

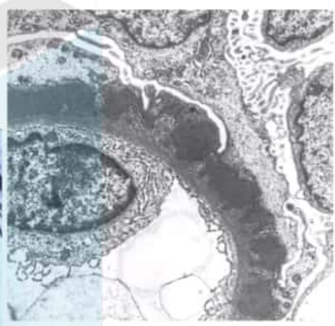


Crescentric glomerulonephritis showing characteristic wrinkling of GBM with focal disruptions (arrows)

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS (MPGN).

This silver stain demonstrates a **double contour** to many basement membranes, or the "tram-tracking" that is characteristic of membranoproliferative glomerulonephritis (MPGN) that results from basement membrane reduplication.





Electron micrograph showing electron-dense deposits *(arrow)* along the epithelial side of the basement membrane

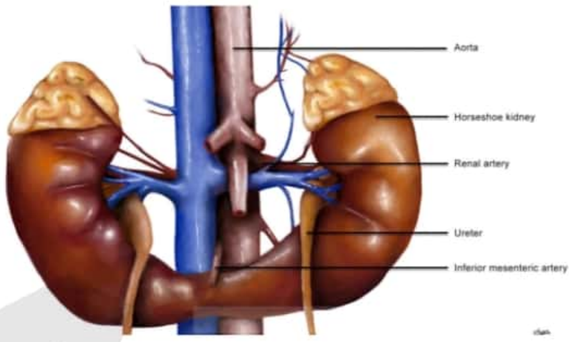
HISTORICAL CLASSIFICATION	MPGN Type I	MPGN Type II or Dense Deposit Disease (DDD)	MPGN Type III
LIGHT MICROSCOPY	Mesangial proliferation with mesangial interposition and GBM duplications (MPGN pattern)	Diverse glomerular histology with or without MPGN pattern	MPGN pattern, usually with membranous features
ELECTRON MICROSCOPY	Mesangial and subendothelial deposits	Mesangial and intramembranous highly electron dense deposits	Mesangial, subendothelial, subepithelial, and/or intramembranous deposits
IMMUNOFLUOROSCENCE	C3 **with** IgG and/or IgM, C1 / **C3 alone**	**C3 alone**	**C3 alone** / C3 **with** IgG and/or IgM, C1
MODERN CATEGORIES	MPGN Type I	C3GN / DDD / C3GN → C3 GLOMERULOPATHY	MPGN Type III

UROLOGY

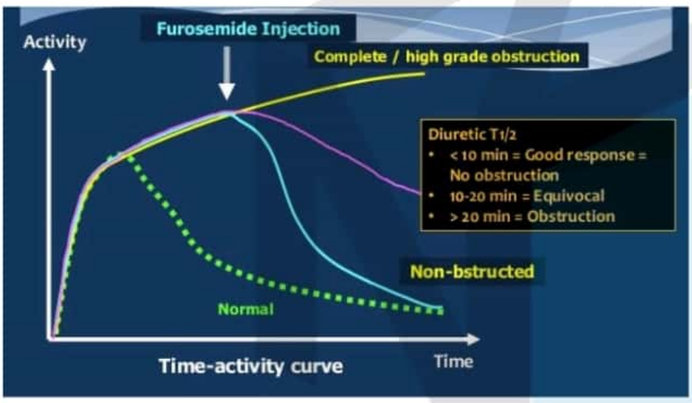
High Yield topics: Renal Stones, Obstruction, UDT, VUR, Transplant, Duplication

Horse-shoe kidney

- Ascent is prevented by the Inferior mesenteric artery
- Isthmus lies at L3-L4
- Pelvis and PUJ lie anteriorly
- M/C fusion abnormality of the kidney



Diuretic Renogram

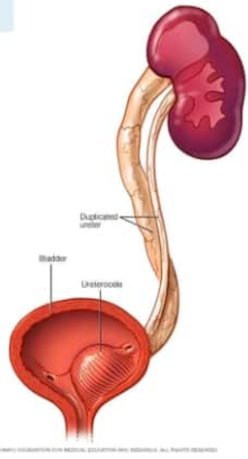


UPJ obstruction

- M/C Cause of congenital hydronephrosis
- Dietel's crisis is seen in intermittent PUJO
- TOC: Dismembered (Anderson-Hyne's) Pyeloplasty
- If function <10% : Nephrectomy

Ureter Duplication

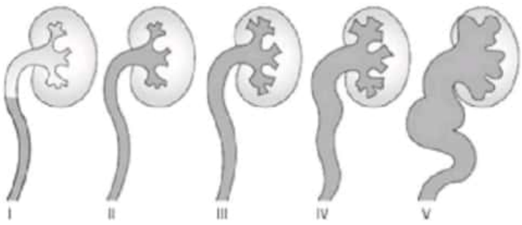
- A/w Weigert-Meyer's rule: In a complete ureteral duplication, the ureter whose orifice is more medial and caudal reaches the upper moiety and the other ureter whose orifice is more lateral and cephalad reaches the lower renal moiety
- Partial > Complete, F>M
- Left > Right
- Lower moiety ureter: prone for reflux (because of short intramural tunnel)
- Upper moiety ureter: Opens in urethra
  - Males- prostatic urethra: continent
  - Females: anterior urethra: incontinence



Ques- 2 year old female with c/o recurrent UTI. MCU is given. What to do next.

Dx: Grade 5 Vesico-ureteric reflux (VUR)

a



b

Grade	Description
I	Into a nondilated ureter
II	Into the pelvis and calyces without dilatation
III	Mild to moderate dilatation of the ureter, renal pelvis, and calyces with minimal blunting of the fornices
IV	Moderate ureteral tortuosity and dilatation of the pelvis and calyces
V	Gross dilatation of the ureter, pelvis, and calyces; loss of papillary impressions; and ureteral tortuosity

Complications: Renal scars
Inv for scars: DMSA Scan

- Spontaneous resolution depends on Grade & Age of presentation both
- Scars occur M/C at Upper pole
- 1st Line t/t: Antibiotic Prophylaxis
- Surgical TOC: Ureteric reimplant (Cohen's) (Indication-breakthrough infection)
- For lower grades you can try DEFLUX- Injection of dextranomer hyaluronic acid copolymer just beneath the ureteric orifice, which is a bulking agent.

Staghorn Stone

- TOC- Percutaneous Nephrolithotomy (PCNL)
- Struvite stone (Triple Phosphate) – Calcium, magnesium, ammonium
- Infection stones- formed in alkaline urine
- M/C Organism- Proteus
- Organism which cannot cause: E. coli as it is found in acidic urine.

Steinstrasse

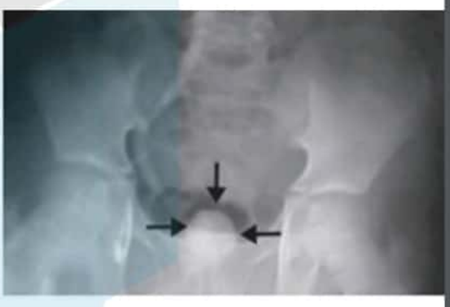
- German word for "stone street", describing a possible complication of extracorporeal shock wave lithotripsy (ESWL) for urinary tract calculi, wherein a column of stone fragments forms that blocks the ureter.

- ESWL:
  - Principle complication of ESWL: infection
  - Other common complication: Hematuria
  - C/I for ESWL: Pregnancy, morbid obesity, distal obstruction
  - M/C Complication of PCNL: Bleeding

TURP procedure

- M/C Complication: Retrograde ejaculation d/t invariable resection of internal sphincter of bladder.
- Irrigant of choice: 1.5 % Glycine
- NS can be used in a bipolar TURP
- Landmark for resection: Veru montanum
- TOC for <30cc prostate: TUIP/BNI (Bladder Neck incision)
- TOC for >80cc prostate: HoLEP (Holmium Laser Enucleation of Prostate)

Thimble Bladder



- Seen in GU Tuberculosis
- Small, contracted thumb like bladder
- GU TB:
  - Route of spread: Hematogenous
  - Primary organs affected: Kidney, Epididymis and Prostrate
  - 1st site: peri-glomerular capillaries.

← PUTTY Kidney or CEMENT Kidney

Seen in Renal TB

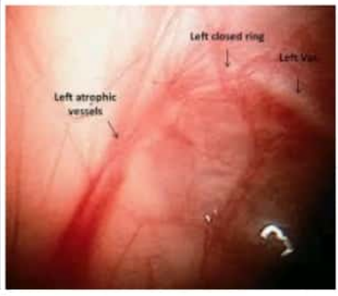
Commonly seen on CT

IOC for Urinary TB: CT Urography

Acute pyelonephritis →

CT Scan: Swollen kidney with striations (Streak Necrosis)

Ques- Diagnostic Laparoscopy finding in a child with left Undescended testis (UDT)

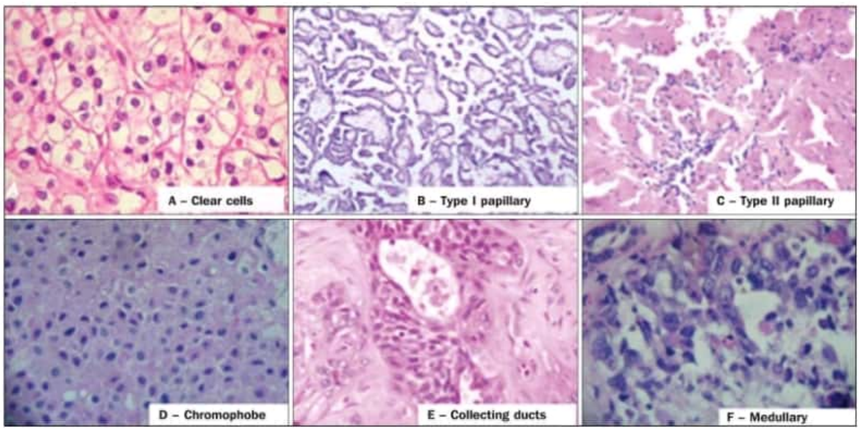


What to do next?

- IOC for UDT: Palpation
- IOC for non-palpable UDT: Diagnostic Laparoscopy
- TOC: Orchidopexy
- Dx in this case: Vanishing testes
- Testicular regression syndrome (TRS) or 'vanishing testis' is a condition which is considered to be due to the subsequentatrophy and disappearance in fetal life of an initially normal testis. The presence of spermatic cord structures is evidence of thepresence of the testis in early intrauterine life.
- Mx in Vanishing testes: Nothing to be done
- MC Malignancy in UDT: Seminoma
- Ideal time for orchidopexy: 6 months
- High (deep ring and proximal): 2 stage Stephen Fowler's orchidopexy

Renal Cell Carcinoma

- Any enhancing renal mass should be considered RCC unless proved otherwise
- RCC can be diagnosed on CT findings and does not necessarily needs a biopsy
- Treatment according to the TNM staging
- If ipsilateral adrenal involved- T4
- If C/L adrenal involved- M1
- Routine LN dissection NOT required (spread is hematogenous)
- DOC for metastatic RCC: Sunitinib/Pazopanib (Tyrosine Kinase inhibitors)



- Clear Cell RCC: 3p deletion or VHL mutation.
  - Loss of HIF (Hypoxia inducing factor)
  - Arise from PCT
- Papillary RCC- Trisomy 7, 17 and loss of chromone Y (in males)
  - a/w Familial papillary RCC – Trisomy 7
  - arises from DCT
- Chromophobe- perinuclear halo + thick cell membrane (plant cell appearance)
  - Arises from intercalated cells of CD
  - Good prognosis
- Xp11 RCC- Histological morphology of both Papillary and clear cell RCC
  - a/w Xp11 (TFE Gene) translocation with various chromosomes
  - more common in children

Subtype	Incidence	Origin, histology	Patients' age	Signal/density pattern	Biological behaviour	hemodynamic pattern	Associations and predisposition
Clear cell	75%	Proximal nepron, tubular epithelium	> 50 years	Heterogeneous density/signal	Aggressive, according to the stage, Furhman grade and sarcomatoid transformation	Hypervascular	Von Hippel-Lindau (2 45%), tuberous sclero (2%)
Papillary	10%	Distal nephron, tubular epithelium	> 50 years	Low T2 signal, hypodense	Aggressive, according to the stage, Furhman grade and sarcomatoid transformation	Hypovascular	Hereditary papillary R
Chromophobe	5%	Distal nephron, intercalated cells of the distal tubules	> 50 years	Hypodense, intermediate signal intensity	Low mortality (10%)	Hypovascular	Birt-Hogg-Dubé s drome (in associat with oncocytomas)
Cystic-solid	1–4%	Similar to renal clear cell carcinoma, without solid nodules	Fourth and fifth decades of life	High T2 signal intensity, fluid density	Indolent, without metastases	Septal and solid portions enhancement	Predominance in me
Collecting ducts (Bellini)	1%	Collecting tubules	> 50 years	Low T2 signal, heterogeneous	Very aggressive, mortality: 70% in two years	Hypovascular	Subtle predominance men
Medullary	1%	Distal nephron	Second and third decades of life	Heterogeneous,infiltrating	Extremelly aggressive	Hypovascular	Associated with sic cell disease
Xp11 translocation	Rare	Distal/proximal nephron, may be similar to papillary or clear cell carcinoma	Children (early childhood)	Hypodense, intermediate T2 signal intensity	Indolent	Hypovascular	TFE3 gene involved the tumor genesis
Mucinous tubular and spindle cell	Rare	Distal nephron, tubular cells	Fourth and fifth decades of life	Subtle T2 hypersignal, central scar may be observed	Slow-growing, rare metastases	Hypovascular	Predominance in wom
Associated with neuroblastoma	Rare	Proximal tubular epithelium	Adolescerice (mean 13 years)	Hypodense, intermediate T2 signal intensity	Indolent	Hypovascular	Previous history of n roblastoma
Non classified	4–6%	Variable	Variable	Variable	High mortality	Variable	—

Ques. 60 year old male smoker with painles gross hematuria.
TURBT report- high grade urothelial cancer, involves muscularis propria.
What next?

Dx: Bladder Cancer

- Evaulation by cystoscopy, cytology and CT scan
- Stage here- T2
- Treatment here- Radical cystectomy
- TOC for Ca in situ- intravesical BCG
- Gold standard and MC used diversion:
  ileal conduit
- Electrolyte abnormalities d/t diversion:
  - Stomach: hypochloremic hypokalemic alkalosis
  - Colon>Ileum: Hyperchloremic hypokalemic acidosis

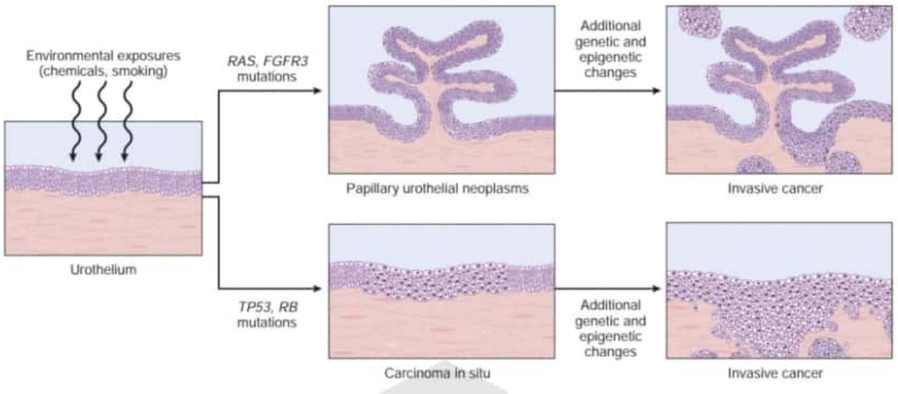
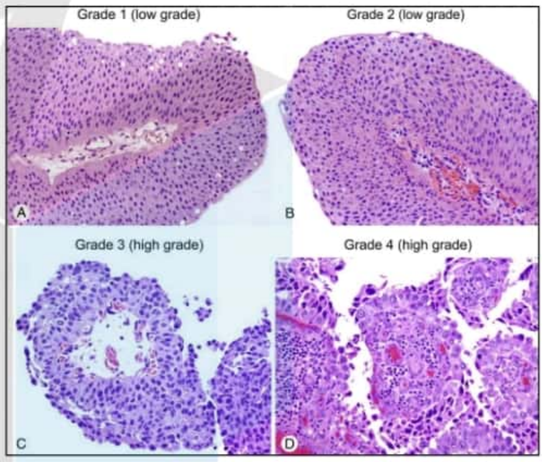


Table 21.3 Tumors of the Urinary Bladder

Urothelial (transitional) tumors
- Noninvasive urothelial (transitional cell) tumors
- Infiltrating urothelial carcinoma
- Variants: nested, microcystic, micropapillary, plasmacytoid, sarcomatoid, giant cell, poorly differentiated, lipid-rich, and clear cell

Adenocarcinoma
Squamous cell carcinoma
Mixed carcinoma
Small-cell carcinoma
Sarcomas



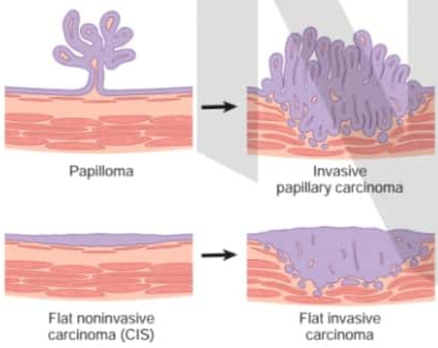


Table 2. Urinary Markers Approved by the US Food & Drug Administration

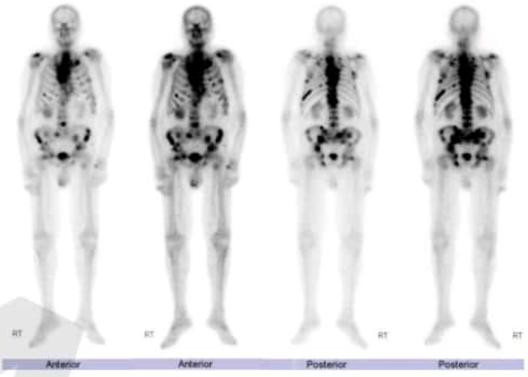
TRADE NAME	MARKER TYPE	ASSAY TARGET	COMMERCIALLY AVAILABLE IN US
NMP-2268	Protein based	Nuclear matrix protein 22	Yes
BTA TRAK/BTA stat69	Protein based	Complement factor H-related protein	No
UroVysion FISH23	Cell based (chromosomal)	Fluorescent probes detect alterations of chromosomes 3, 7, 9p21, and 17	Yes
ImmunoCyt70	Cell based (immunologic)	Monoclonal antibodies against HMW-CEA and 2 forms of cytoplasmic mucin	No
CxBladder27	mRNA based	Detection of IGFBP5, HOXA13, MDK, CDK1, and CXCR2 mRNAs	Yes

All tests are performed on voided urine specimens. HMW-CEA = high-molecular weight carcinoembryonic antigen; FISH = fluorescence in situ hybridization.

© 2018 Digital Science Press, Inc. and UroToday.com

Ques. 65 year old male with poor urine flow and back pain. DRE shows hard nodular prostate. PSA is 150 ng/ml, biopsy- Gleason 8. Bone scan shows multiple mets. Treatment?

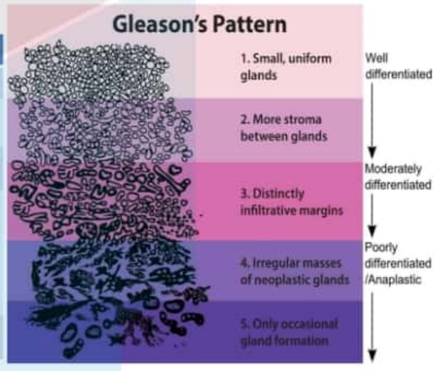
Dx: Ca Prostate



- Treatment: Hormonal ablation (androgen deprivation therapy)
- MC from peripheral zone
- Mets are MC to Lumbar Vertebrae (OSTEOBLASTIC)
- Spread via valveless Batson Venous plexus.
- Active Surveillance for 'Low Risk' patients:
  - Gleason <= 6
  - PSA <= 10 ng/mL
  - Stage <= T2a

GLEASON'S SCORE

New category	Histological descriptions of new grading categories
Grade 1	• Only individual, discrete well-formed glands
Grade 2	• Predominantly well-formed glands with lesser component of poorly formed, fused, and/or cribriform glands
Grade 3	• Predominantly poorly formed poorly formed, fused, and/or cribriform glands with lesser component of well-formed glands
Grade 4	• ***Only*** poorly formed, fused, and/or cribriform glands ***or*** • Predominantly well-formed glands with lesser component lacking gland formation ***or*** • Predominantly lacking gland formation and lesser component of well-formed glands (but poorly formed, fused, and/or cribriform glands can be a minor component)
Grade 5	• Lacks gland formation – or has glands with necrosis -- with or without poorly formed, fused, and/or cribriform glands



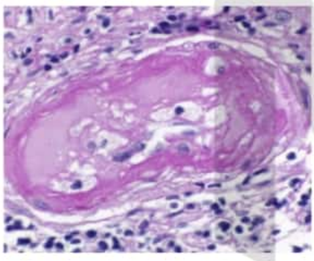
- Grade 1/2/3- Well Formed glands
- CRIBRIFORM pattern is NOW given a Grade 4 directly (Cribriform cancer no longer qualifies as Gleason 3, even if the glands are similar in size to normal glands)
- Grade 5: Single cell/ Comedo Necrosis

- Gleason **score** is the sum of the two most prevalent Gleason **grades**: primary (largest) and secondary (2nd Largest), designated according to separate rules for biopsy and prostatectomy
- If only one pattern is present, the primary and secondary patterns are given the same grade (ex: 3+3=6)
- **Systematic** needle biopsy sets contain cores from different anatomically designated sites
  - Gleason score should be assigned separately for each anatomically designated site
  - Highest score may serve as a basis to determine treatment
- Any glands showing perineural invasion must be excluded in assigning Gleason grading because perineural invasion distorts gland morphology such that Gleason 3 glands resemble Gleason 4

Transplant Rejection

Transplant Rejection				
	Type	Onset	Mechanism & Vessel Histology	Type of Hypersensitivity
"Host vs. Graft"	Hyperacute	Immediate	**Preformed antibodies** directed against the donor tissue. Caused by accidental ABO **blood type incompatibility** which is very rare. Presents while still in surgery with **thrombosis and occlusion** of graft vessels	II
"Host vs. Graft"	Acute	Weeks to months	T-Cell mediated immune response directed against the foreign MHC. Inflammation and **leukocyte infiltration of graft vessels** results. Most common type.	IV
"Host vs. Graft"	Chronic	Months to years	T-Cell mediated process resulting from the foreign MHC "looking like" a self MHC carrying an antigen. Results in **intimal thickening and fibrosis of graft vessels** as well as graft atrophy	III & IV
Graft vs. Host		Varies	Donor T-Cells in the graft proliferate and attack the recipient's tissue. Most commonly seen in **bone marrow transplants**. Presents with **diarrhea, rash and jaundice**.	IV

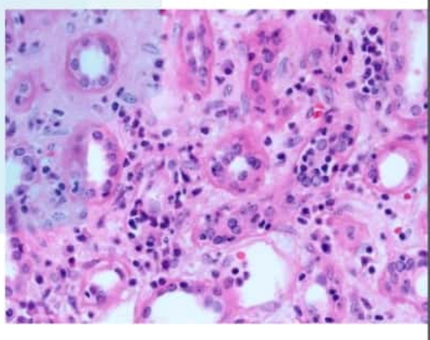
* The most important thing to remember is the timeframe for the onset of symptoms as you can often determine what type of rejection it is based on time alone

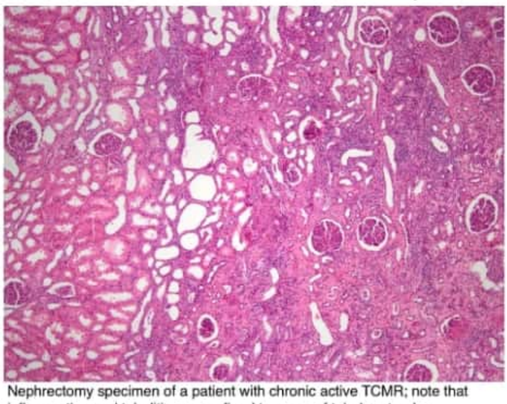


← Fibrinoid Necrosis seen in hyperacute kidney rejection (specially in Humoral rejection) (sometimes acute also)

Tubulitis (empty tubules) with infiltrates →

Marker of T cell mediated rejection (TCMR) in kidney (Chronic Rejection)





Nephrectomy specimen of a patient with chronic active TCMR; note that inflammation and tubulitis are confined to areas of tubular atrophy

M/C Rejection: Chronic Cell-mediated

2nd M/C: Acute Cell mediated

Immunosuppressives don't work in hyperacute rejections

R/F: Multiple pregnancies, blood transfusions

Immunosuppressants used in Kidney Transplant

A. Induction immunosuppressive therapy

- Induction therapy should consist of an antibody plus standard immunosuppressive therapy.
- Advantages- Prevents acute rejection & lower the need of steroid dose.
- Best time to start is 1-2 days before transplant.
- Antibodies include rabbit anti-thymocyte globulin (rATG)- Thymoglobulin, alemtuzumab, and basiliximab.
- ALEMTUZUMAB- CD52 inhibitor
- BASILIXIMAB- IL2 Receptor Inhibitor (CD25)

- Patients with High Risk for Rejection – There is substantial evidence that rabbit antithymocyte globulin (rATG)- Thymoglobulin is superior to IL-2 Receptor Antibodies.
- Patients with Low Risk for Rejection – rATG Thymoglobulin produces and IL-2 receptor antagonist have shown similar rates of acute rejection, patient and graft survival.

Induction agent

No induction < Basiliximab < Alemtuzumab < Anti-thymocyte globulin

Lower risk	Higher risk
Zero HLA mismatch	Increased tt of HLA mismatche
Live donor	Younger recipient and older donor age
Caucasian ethnicity	African-American ethnicity
Low panel reactive antibody	High panel reactive antibody
Absence of donor specific antibody	Presence of donor specific antibody
Blood group compatibility	Blood group incompatability
Immediate graft function	Delayed onset of graft function
Short cold ischemia time	Long cold ischemia time
First transplant	Retransplant

Notable exceptions:

- Patient unable to tolerate rATG- Thymoglobulinm, d/t hypotension, leukopenia and/or thrombocytopenia. Basiliximab is preferred.
- Caucasians recipients of two-haplotypes-identical, living, related kidneys due to decreased immunologic risk of acute rejection.
- Recipients who have another functioning solid organ transplant such as a liver, lung or heart and who are currently being administered immunosuppressive drugs.

B. Maintenance immunosuppressive therapy

- A maintenance regimen consisting of **triple** immunosuppression therapy with a calcineurin inhibitor, an antimetabolite and prednisolone is recommended for lifelong.
- Among calcineurin inhibitor, TACROLIMUS is preferred over CYCLOSPORINE as TACROLIMUS is a/s decreased acute rejection rates and is generally better tolerated than cyclosporine.

TABLE 307-3 Maintenance Immunosuppressive Drugs

AGENT	PHARMACOLOGY	MECHANISMS	SIDE EFFECTS
Glucocorticoids	Increased bioavailability with hypoalbuminemia and liver disease; prednisone/prednisolone generally used	Binds cytosolic receptors and heat shock proteins. Blocks transcription of IL-1, -2, -3, -6, TNF-α, and IFN-γ	Hypertension, glucose intolerance, dyslipidemia, osteoporosis
Cyclosporine (CsA)	Lipid-soluble polypeptide, variable absorption, microemulsion more predictable	Trimolecular complex with cyclophilin and calcineurin → block in cytokine (e.g., IL-2) production; however, stimulates TGF-β production	Nephrotoxicity, hypertension, dyslipidemia, glucose intolerance, hirsutism/hyperplasia of gums
Tacrolimus	Macrolide, well absorbed	Trimolecular complex with FKBP-12 and calcineurin → block in cytokine (e.g., IL-2) production; may stimulate TGF-β production	Similar to CsA, but hirsutism/hyperplasia of gums unusual, and diabetes more likely
Azathioprine	Mercaptopurine analogue	Hepatic metabolites inhibit purine synthesis	Marrow suppression (WBC > RBC > platelets)
Mycophenolate mofetil/sodium	Metabolized to mycophenolic acid	Inhibits purine synthesis via inosine monophosphate dehydrogenase	Diarrhea/cramps; dose-related liver and marrow suppression is uncommon
Sirolimus/Everolimus	Macrolide, poor oral bioavailability	Complexes with FKBP-12 and then blocks p70 S6 kinase in the IL-2 receptor pathway for proliferation	Hyperlipidemia, thrombocytopenia
Belatacept	Fusion protein, intravenous injections	Binds CD80 and CD86, prevents CD28 binding and T cell activation	Posttransplant Lymphoproliferative Disease (PTLD)

Abbreviations: FKBP-12, FK506 binding protein 12; IFN, interferon; IL, interleukin; RBC, red blood cells; TGF, transforming growth factor; TNF, tumor necrosis factor; WBC, white blood cells.

- Among antimetabolic agents, Mycophenolate is preferred over azathioprine because of its superior ability to prevent acute rejection and its better side effect profile.
- Mycophenolate is teratogenic and more costly, and hence azathioprine is preferred in these special cases.
- In most kidney transplant recipients, a stable maintenance immunosuppression regimen is established within the first three months after transplantation.
- Complete withdrawal of all maintenance therapy is **not** recommended, since it frequently lead to late acute rejection or accelerated chronic rejection.

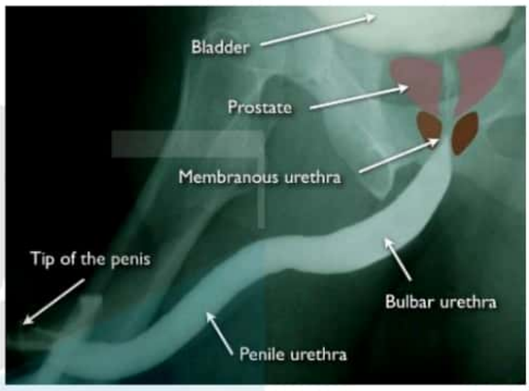
Treatment of antibody mediated rejection (ABMR) of the renal allograft

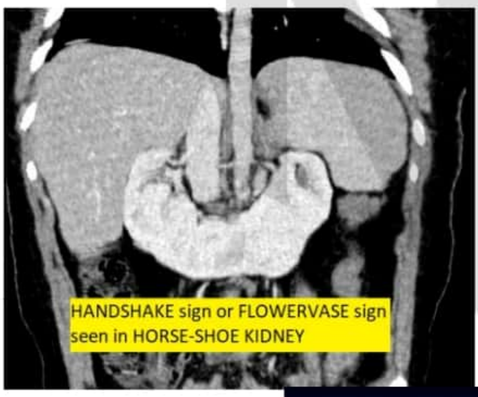
- ABMR is the M/C cause of allograft failure after kidney transplant
- Patients with active ABMR are at increased risk for subsequent rejection, chronic ABMR and graft loss
- The primary goal of treating ABMR is to remove existing donor specific antibodies and to eradicate the clonal population of B cells or plasma cells that is responsible for their production.

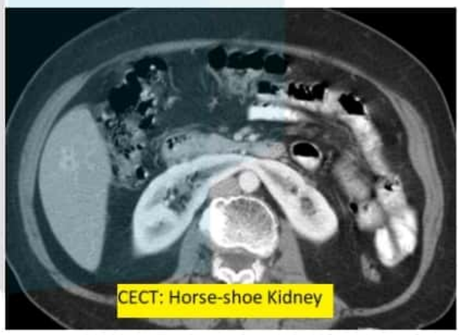
- Plasmapheresis
- Immunoglobin infusions
- Anti-CD20 monoclonal antibodies (RITUXIMAB) to target B lymphocytes
- BORTEZOMIB to target antibodies producing plasma cells
- ECULIZUMAB to inhibit complement- C5
- Anti-CD3 monoclonal antibody (OKT3)

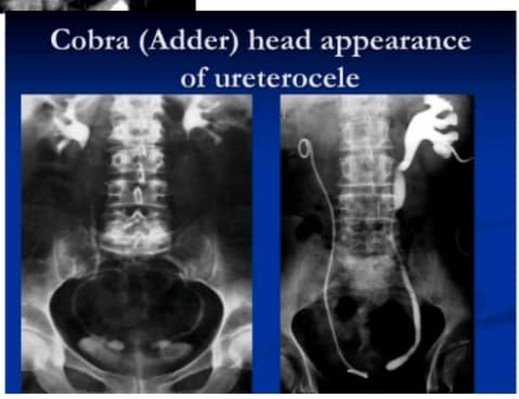
Urethral Stricture (seen on RGU)

- Stricture of bulbar urethra (M/C site)
- TOC for nontraumatic short segment strictures- INTERNAL URETHROTOMY
- TOC for traumatic stricture: Urethroplasty
  - <2cm- anastomotic
  - >2cm- augmentation (commonly by buccal mucosa)









Fish hook ureter

- S shaped ureter
- Right sided fish hook ureter → right ureter hooks behind IVC **(RETROCAVAL URETER)**
  - **Developmental anomaly of IVC**
  - **Persistent right posterior cardinal V→ therefore ends passing infront of ureter**

aka Revere J sign

IVP demonstrating the characteristic stretching of calyces by cysts in polycystic kidneys.

Spider leg appearance

CT SCAN in ADPCKD patient
Do MR-Angio in brain to screen for cerebral anerysms

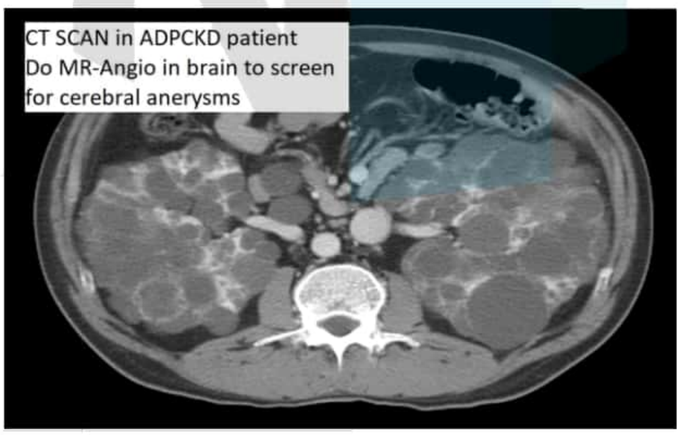


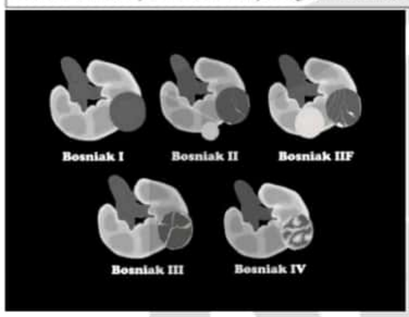
Table 4: Suggested Terms and Phrases to Use When Reporting Cystic Renal Masses Using the Bosniak Classification, Version 2019

Classification	Suggested Terms and Phrases
Bosniak I	"Benign simple renal cyst requiring no follow-up."
Bosniak II	(Option 1) "Benign Bosniak II renal cyst requiring no follow-up."* (Option 2) "Likely benign Bosniak II renal mass requiring no follow-up."†
Bosniak IIF	"Bosniak IIF cystic renal mass. The large majority of Bosniak IIF masses are benign. When malignant, nearly all are indolent. Generally, Bosniak IIF masses are followed by imaging at 6 months and 12 months, then annually for a total of 5 years to assess for morphologic change."
Bosniak III	"Bosniak III cystic renal mass. Bosniak III masses have an intermediate probability of being malignant. If not already obtained, consider urology consultation."
Bosniak IV	"Bosniak IV cystic renal mass. The large majority of Bosniak IV masses are malignant. If not already obtained, consider urology consultation."

Note.—This content is intended for patients in the general population and not those with a renal cell carcinoma syndrome.

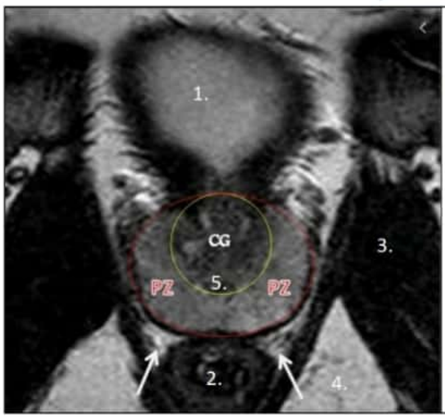
* This option is best used for Bosniak II masses that have been confirmed to be cysts (eg, cysts with few thin septa).

† The Bosniak II category includes some masses that, although they are reliably considered benign, have not been definitively characterized as cysts (eg, low-attenuation lesions that are too small to characterize).



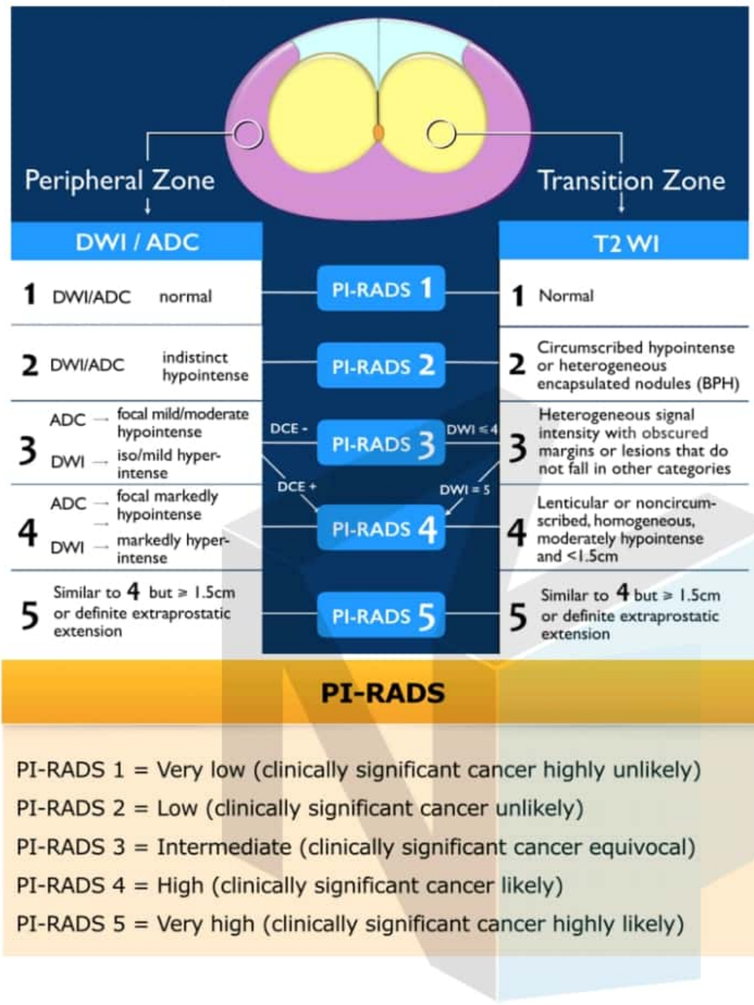
DROOPING LILY SIGN

Appearance of lower pole calyces in a duplicated collecting system with non functioning of upper pole.



MRI PROSTATE- ANATOMY

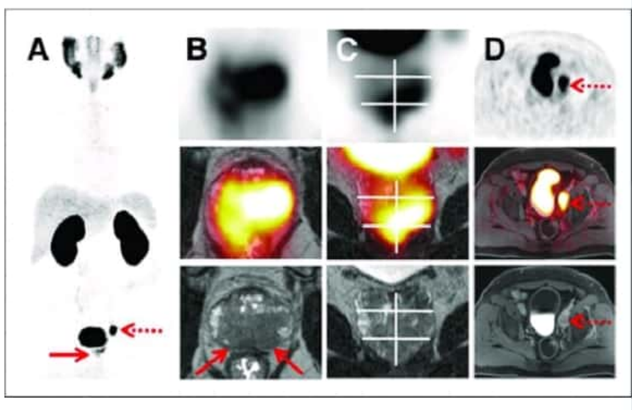
1. Bladder
2. Rectum
3. Obturator internus
4. Ischiorectal Fossa
5. Prostate

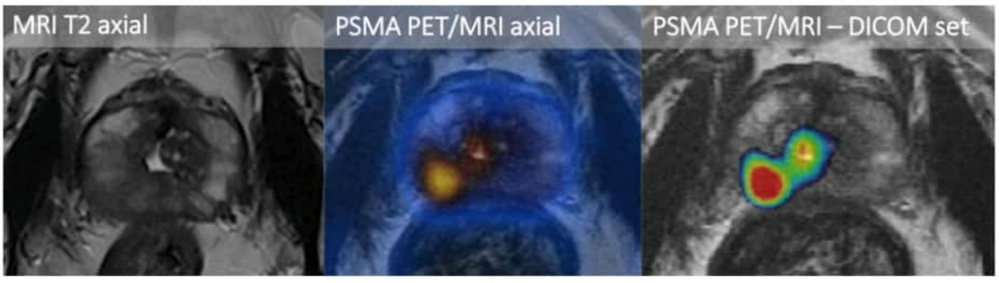

Peripheral Zone
Transition Zone
DWI / ADC
T2 WI
1 DWI/ADC normal
PI-RADS 1
1 Normal
2 DWI/ADC indistinct hypointense
PI-RADS 2
2 Circumscribed hypointense or heterogeneous encapsulated nodules (BPH)
3 ADC → focal mild/moderate hypointense
DWI → iso/mild hyperintense
DCE -
DWI ≤ 4
PI-RADS 3
3 Heterogeneous signal intensity with obscured margins or lesions that do not fall in other categories
4 ADC → focal markedly hypointense
DWI → markedly hyperintense
DCE +
DWI = 5
PI-RADS 4
4 Lenticular or noncircumscribed, homogeneous, moderately hypointense and <1.5cm
5 Similar to 4 but ≥ 1.5cm or definite extraprostatic extension
PI-RADS 5
5 Similar to 4 but ≥ 1.5cm or definite extraprostatic extension

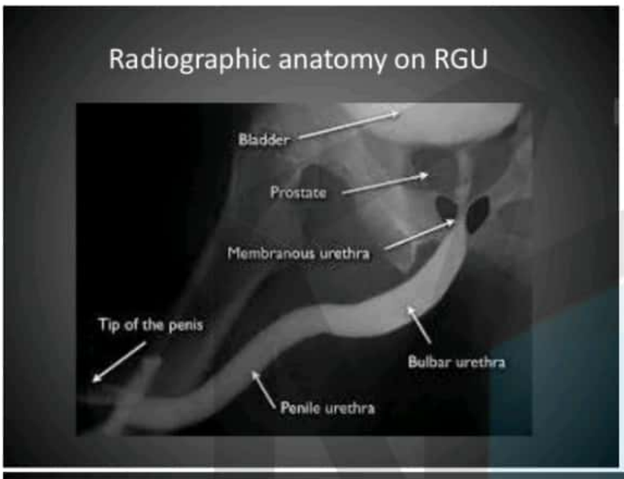
PI-RADS

PI-RADS 1 = Very low (clinically significant cancer highly unlikely)
PI-RADS 2 = Low (clinically significant cancer unlikely)
PI-RADS 3 = Intermediate (clinically significant cancer equivocal)
PI-RADS 4 = High (clinically significant cancer likely)
PI-RADS 5 = Very high (clinically significant cancer highly likely)

Gallium 68- PSMA PET MRI used in **prostate cancer**







On RGU: only small amount of bladder can be seen, not the full view seen in MCU

On MCU: Bladder is always full

Micturating cystourethrogram (MCU)/Anterior Uretherography

INDICATIONS :-

CHILDREN

- UTI
- Voiding difficulties.
- Vesico-ureteric reflux.
- Baseline study prior to urinary tract surgery.
- Post operative evaluation of ureteric abnormalities.
- Trauma.
- Suspected anatomic abnormalities of bladder neck & urethra. (posterior urethral valve)

ADULTS

- Functional disorders of bladder & urethra.
- Suspected vesicovaginal / vesicocolic fistula.
- Suspected bladder / urethral trauma.
- Urethral diverticula

NORMAL MCU